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=> s (phosphatidylch? or PC) (2N) chol? (2n) (ps or phosphatidylser?)

L1 501 (PHOSPHATIDYLCH? OR PC) (2N) CHOL? (2N) (PS OR PHOSPHATIDYLSER?)

=> s (glycoprot? or asialoglycoprot?)

L2 602312 (GLYCOPROT? OR ASIALOGLYCOPROT?)

=> s l1 and l2

L3 27 L1 AND L2

=> dup rem l3

PROCESSING COMPLETED FOR L3

L4 9 DUP REM L3 (18 DUPLICATES REMOVED)

=> s l4 and (py=<2001)

2 FILES SEARCHED...

L5 8 L4 AND (PY=<2001)

=> s WONG, J?/au

L6 12691 WONG, J?/AU

=> s tsang, s?/au

L7 1350 TSANG, S?/AU

=> s l6 or l7

L8 14040 L6 OR L7

=> s l8 and l1 and l2

L9 0 L8 AND L1 AND L2

=> s l8 and l1

L10 1 L8 AND L1

=> s l8 and l2

L11 95 L8 AND L2

=> s l10 and l5

L12 0 L10 AND L5

=> s l10 or l5

L13 9 L10 OR L5

=> d l13 ibib abs 1-9

L13 ANSWER 1 OF 9 MEDLINE on STN  
ACCESSION NUMBER: 1999400476 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 10471286  
TITLE: Effect of nonpolar substitutions of the conserved Phe11 in the fusion peptide of HIV-1 gp41 on its function, structure, and organization in membranes.  
AUTHOR: Pritsker M; Rucker J; Hoffman T L; Doms R W; Shai Y  
CORPORATE SOURCE: Department of Biological Chemistry, Weizmann Institute of Science, Rehovot, Israel.  
SOURCE: Biochemistry, (1999 Aug 31) 38 (35) 11359-71.  
Journal code: 0370623. ISSN: 0006-2960.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals; AIDS  
ENTRY MONTH: 199909  
ENTRY DATE: Entered STN: 19991012  
Last Updated on STN: 19991012  
Entered Medline: 19990928

AB The fusion domain of the HIV-1 envelope **glycoprotein** (gp120-gp41) is a conserved hydrophobic region located at the N-terminus of the transmembrane subunit (gp41). A prominent feature of this domain is a conserved five-residue "FLGFL" sequence at positions 8-12. Mutation of the highly conserved Phe(11) to Val (F11V), presumed not to significantly affect the hydrophobicity and the structure of this region, has been shown to decrease the level of syncytium formation and virus infectivity. Here we show that the substitution of Gly for Phe(11) (F11G) reduces cell-cell fusion activity by 80-90%. To determine the effect of these mutations on the properties of the fusion peptide, a 33-residue peptide (WT) identical to the extended fusion domain and its F11V and F11G mutants were synthesized, fluorescently labeled, and studied with respect to their function, structure, and organization in phospholipid membranes. The WT peptide alone induced fusion of both zwitterionic (PC/Chol) and negatively charged (**PS/PC/Chol** and POPG) vesicles, in contrast to a 23-mer fusion peptide lacking the C-terminal domain which has been shown to be inactive with PC vesicles but able to induce fusion of POPG vesicles which had been preaggregated with Ca(2+) or Mg(2+). The F11V peptide preserved 50% activity, and the F11G peptide was virtually inactive. ATR-FTIR spectroscopy indicated similar secondary structure of the peptides in multibilayers that was independent of membrane composition. Furthermore, all the peptides increased the extent of lipid disorder to a similar extent, but the kinetics of amide II H to D exchange was in the following order: F11G > F11V > WT. Fluorescence studies in the presence of membranes, as well as SDS-PAGE, revealed that the WT and F11V peptides self-associate to similar levels while F11G exhibited a decreased level of self-association. The data suggest that the FLGFL motif contributes to the functional organization of the HIV-1 fusion peptide and that the C-terminal domain following the fusion peptide contributes to the membrane fusion process.

L13 ANSWER 2 OF 9 MEDLINE on STN  
ACCESSION NUMBER: 96107216 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 8530492  
TITLE: pH-dependent conformational properties of saposins and their interactions with phospholipid membranes.  
AUTHOR: Vaccaro A M; Ciaffoni F; Tatti M; Salvioli R; Barca A; Tognozzi D; Scerch C  
CORPORATE SOURCE: Department of Metabolism and Pathological Biochemistry, Istituto Superiore Sanita, Rome, Italy.

SOURCE: Journal of biological chemistry, (1995 Dec 22)  
270 (51) 30576-80.  
Journal code: 2985121R. ISSN: 0021-9258.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199601  
ENTRY DATE: Entered STN: 19960220  
Last Updated on STN: 20000303  
Entered Medline: 19960130

AB Saposins A, B, C, and D are small lysosomal **glycoproteins** released by proteolysis from a single precursor polypeptide, prosaposin. We have presently investigated the conformational states of saposins and their interaction with membranes at acidic pH values similar to those present in lysosomes. With the use of phase partitioning in Triton X-114, experimental evidence was provided that, upon acidification, saposins (Sap) A, C, and D acquire hydrophobic properties, while the hydrophilicity of Sap B is apparently unchanged. The pH-dependent exposure of hydrophobic domains of Sap C and D paralleled their pH-dependent binding to large unilamellar vesicles composed of **phosphatidylcholine, phosphatidylserine, and cholesterol**. In contrast, the binding of Sap A to the vesicles was very restricted, in spite of its increased hydrophobicity at low pH. A low affinity for the vesicles was also shown by Sap B, a finding consistent with its apparent hydrophilicity both at neutral and acidic pH. At the acidic pH values needed for binding, Sap C and D powerfully destabilized the phospholipid membranes, while Sap A and B minimally affected the bilayer integrity. In the absence of the acidic phospholipid phosphatidylserine, the induced destabilization markedly decreased. Of the four saposins, only Sap C was able to promote the binding of glucosylceramidase to phosphatidylserine-containing membranes. This result is consistent with the notion that Sap C is specifically required by glucosylceramidase to exert its activity. Our finding that an acidic environment induces an increased hydrophobicity in Sap A, C, and D, making the last two saposins able to interact and perturb phospholipid membranes, suggests that this mechanism might be relevant to the mode of action of saposins in lysosomes.

L13 ANSWER 3 OF 9 MEDLINE on STN  
ACCESSION NUMBER: 95306170 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 7786607  
TITLE: Failure of liposomal encapsulation of doxorubicin to circumvent multidrug resistance in an in vitro model of rat glioblastoma cells.  
AUTHOR: Hu Y P; Henry-Toulme N; Robert J  
CORPORATE SOURCE: Fondation Bergonie, Bordeaux, France.  
SOURCE: European journal of cancer (Oxford, England : 1990), (1995) 31A (3) 389-94.  
Journal code: 9005373. ISSN: 0959-8049.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199507  
ENTRY DATE: Entered STN: 19950807  
Last Updated on STN: 19970203  
Entered Medline: 19950727

AB We studied the capacity of doxorubicin encapsulation in liposomes of various lipid compositions to circumvent multidrug resistance in several variants of the C6 rat glioblastoma cell line in culture, and to inhibit azidopine binding to membranes isolated from these cells. Three formulations of liposomes were prepared: (a) phosphatidylcholine (PC)/**phosphatidylserine (PS)**/

**cholesterol** (cho) at a 9/24 ratio; (b) PC/cardiolipin (CL)/cho at 10/1/4 ratio; (c) dipalmitoylphosphatidylcholine (DPPC)/cho at 11/4 ratio. Unloaded liposomes presented no cytotoxicity against sensitive or resistant cells. Doxorubicin encapsulated in PC/PS/cho and PC/CL/cho liposomes had a cytotoxic activity close to that of free doxorubicin, whereas doxorubicin encapsulated in DPPC/cho liposomes was significantly less active than free doxorubicin in sensitive as well as in two of the three multidrug resistant cell lines, and as active as free doxorubicin in the third one. Free doxorubicin was able to decrease 50% of [3H]azidopine photolabelling to **P-glycoprotein** at a concentration of 40 microM; doxorubicin encapsulated in PC/CL/cho or PC/PS/cho liposomes was able to inhibit [3H]azidopine binding similarly as free drug, whereas doxorubicin encapsulated in DPPC/cho liposomes had no significant effect on this parameter. Unloaded liposomes of either lipid composition had no effect on [3H]azidopine binding. Together with physical studies performed in parallel on doxorubicin trapping in liposomes (J Liposome Res 1993, 3, 753-766), these results suggest that doxorubicin leaked out of fluid liposomes (PC/PS/cho or PC/CL/cho), whereas rigid liposomes (DPPC/cho) were able to sequester the drug more efficiently. In that case, however, no availability of the drug to the cells was possible and only a weak cytotoxicity was exhibited, especially without any favourable effect on multidrug resistance. In conclusion, no reversal of doxorubicin resistance was found to occur through liposomal encapsulation of the drug.

L13 ANSWER 4 OF 9 MEDLINE on STN  
 ACCESSION NUMBER: 95034813 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 7947787  
 TITLE: Transport studies of doxorubicin in model membranes indicate a difference in passive diffusion across and binding at the outer and inner leaflets of the plasma membrane.  
 AUTHOR: Speelmans G; Staffhorst R W; de Kruijff B; de Wolf F A  
 CORPORATE SOURCE: Department of Biochemistry of Membranes, Utrecht University, The Netherlands.  
 SOURCE: Biochemistry, (1994 Nov 22) 33 (46) 13761-8.  
 Journal code: 0370623. ISSN: 0006-2960.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199412  
 ENTRY DATE: Entered STN: 19950110  
 Last Updated on STN: 19950110  
 Entered Medline: 19941221

AB The kinetics of passive transport of the anticancer drug doxorubicin were analyzed in relation to membrane composition in large unilamellar vesicles in which DNA was enclosed. Special attention was paid to lipids that are typical for the inner and outer leaflet of the plasma membrane of mammalian cells: Phosphatidylethanolamine and anionic **phosphatidylserine** versus **phosphatidylcholine**, sphingomyelin, and **cholesterol**, respectively. The presence of anionic phospholipids results in a highly efficient incorporation of the drug into biological and model membranes [de Wolf, F. A., et al. (1993) Biochemistry 32, 6688-6695]. Therefore, the effect of drug binding on the amount of free, transportable drug was explicitly taken into account. However, even after correction for binding the permeability coefficient was about 35% lower in membranes containing 50 mol % of the anionic phosphatidylserine than in membranes consisting only of zwitterionic phospholipids (0.71-0.79 versus 1.18-1.25 microns s<sup>-1</sup>). This shows that drug binding and insertion also affect the intrinsic transport characteristics of the membranes. As compared to pure phosphatidylcholine, binding was not influenced by the incorporation of sphingomyelin or cholesterol, but equimolar amounts of sphingomyelin and

cholesterol in phosphatidylcholine membranes decreased the rate of doxorubicin transport by 60% and 80%, respectively. The inhibitory effect of these two lipids is probably due to a closer packing of the membranes. In accordance, after the acyl chain order was decreased by adding the anaesthetic-like phenethyl alcohol (0.5% v/v), transport was stimulated more than 4-fold. The implications of our findings for the functioning and rate of drug pumping by the multidrug resistance-conferring P-glycoprotein in cancer cells are discussed.

L13 ANSWER 5 OF 9 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
 ACCESSION NUMBER: 1986:364723 BIOSIS  
 DOCUMENT NUMBER: PREV198682069197; BA82:69197  
 TITLE: VESICULAR STOMATITIS VIRUS BINDS AND FUSES WITH  
 PHOSPHOLIPID DOMAIN IN TARGET CELL MEMBRANES.  
 AUTHOR(S): YAMADA S [Reprint author]; OHNISHI S-I  
 CORPORATE SOURCE: DEP BIOPHYS, FAC SCI, KYOTO UNIV, SAKYO-KU, KYOTO 606, JPN  
 SOURCE: Biochemistry, (1986) Vol. 25, No. 12, pp. 3703-3708.  
 CODEN: BICHAW. ISSN: 0006-2960.  
 DOCUMENT TYPE: Article  
 FILE SEGMENT: BA  
 LANGUAGE: ENGLISH  
 ENTRY DATE: Entered STN: 6 Sep 1986  
 Last Updated on STN: 6 Sep 1986

AB Fusion of vesicular stomatitis virus with some cells (HELR 66, KB, and human erythrocytes, both intact and trypsinized) and liposomes made of various natural and synthetic lipids was studied with spin-labeled phospholipid. Binding of virus was assayed separately with radiolabeled and spin-labeled virus. Binding to cells and liposomes was small at neutral pH but enhanced at acidic pHs. Fusion with cells and liposomes was negligibly small at neutral pH but greatly activated at acidic pHs lower than 6.5. Activation of fusion occurred at lower pH values than enhancement of binding. Fusion occurred rapidly and efficiently, reaching a plateau at 50-80% after 3 min at 37° C. Binding and fusion with cells were enhanced by pretreatment of cells with trypsin. Binding to liposomes was dependent on the head group of the phospholipid, stronger to phosphatidylserine than to phosphatidylcholine, but not much dependent on the acyl chain composition. On the other hand, cis-unsaturated acyl chains were required for the efficient fusion, but there was only a small, if any, requirement for the head group. Cholesterol enhanced the fusion further. High fusion efficiency with cis-unsaturated phospholipids cannot be ascribed to the membrane fluidity but may be related to higher tail-to-head volume ratios. Possible mode of interaction of viral G glycoprotein with phospholipid is discussed. The virus cell entry mechanism is suggested as binding to the phospholipid domain in the cell surface membranes, endocytosis, and followed by fusion with the phospholipid domain in endosomes upon acidification.

L13 ANSWER 6 OF 9 CA COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 134:285583 CA  
 TITLE: Phospholipid liposome formulations  
 INVENTOR(S): Modi, Pankaj  
 PATENT ASSIGNEE(S): Generex Pharmaceuticals, Inc., Can.  
 SOURCE: U.S., 6 pp., Cont.-in-part of U.S. Ser. No. 680,826, abandoned.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6214375	B1	20010410	US 1999-277600	19990329 <--

PRIORITY APPLN. INFO.: US 1996-680826 B2 19960716

AB Liposomes are comprised of a medicinally active agent, at least three phospholipids and at least two biodegradable polymers. The liposomes can be used for delivery of various cosmetics and drugs, and can be administered orally, topically or by injection. An example composition contained egg **phosphatidylcholine**, phosphatidylethanolamine, **cholesterol**, **phosphatidylserine**, and triolein.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 9 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 128:196663 CA

TITLE: Use of virulence factors of pathogens to improve liposomal delivery of antibiotics and/or vaccines

INVENTOR(S): **Wong, Jonathan P.**; Dininno, Vincent L.; Cherwonogrodzky, John W.

PATENT ASSIGNEE(S): Minister of National Defence, Can.

SOURCE: Can. Pat. Appl., 21 pp.

CODEN: CPXXEB

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2171369	AA	19970909	CA 1996-2171369	19960308
US 6221386	B1	20010424	US 1999-251304	19990217
PRIORITY APPLN. INFO.:			CA 1996-2171369	A 19960308
			US 1997-782129	B2 19970113

AB Liposome encapsulated antibiotic therapy has limited application against infectious organisms which can sequester in non-phagocytic cells. Virulence factors of these infectious organisms, for example bacterial components, when used in the formulation of liposomes can enhance the effectiveness of liposomes as delivery systems in the treatment of disease. In this manner, multi-functional liposomes can be developed to treat target diseases. In addition to serving as antibiotic delivery systems, such liposomes also have an immunization effect. Thus, the liposomes can be used for both the prevention and treatment of diseases. Liposome were prepared by dissolving in 2:1 chloroform:methanol the lipids **phosphatidylcholine:cholesterol:phosphatidylserine** in a molar ration of 7:2:1 and the lipid solution was dried. Then 40 µL of a solution of smooth lipopolysaccharides (10 mg/mL) from *Brucella melitensis* was added to the above lipid mixture followed by addition of 2 mL of 20 mg/L ciprofloxacin and heated at 45° while vortexing for 15-25 times. The lipid-antibiotic-lipopolysaccharide mixture was sonicated and freeze-dried to obtain the liposomes of the invention. The protection of mice given multiple doses of above liposomes before infection with *B. melitensis* were studied.

L13 ANSWER 8 OF 9 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 112:75163 CA

TITLE: Immunogenic composites capable of selectively inducing antibody production, pharmaceutical compositions employing the same, and method of selectively inducing antibody production

INVENTOR(S): Mannino, Raphael J.; Goodman-Snitkoff, Gail

PATENT ASSIGNEE(S): Albany Medical College, USA

SOURCE: Eur. Pat. Appl., 30 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 306912	A2	19890315	EP 1988-114597	19880907 <--
EP 306912	A3	19890705		
R: BE, CH, DE, ES, FR, GB, IT, LI, NL, SE				
AU 8821925	A1	19890309	AU 1988-21925	19880907 <--
AU 626797	B2	19920813		
JP 02184635	A2	19900719	JP 1988-316634	19881216 <--
JP 07049376	B4	19950531		
US 6048531	A	20000411	US 1993-160093	19931201 <--
PRIORITY APPLN. INFO.:			US 1987-93660	A 19870908
			US 1991-685986	B1 19910415

AB Immunogenic composites capable of inducing or enhancing antibody production to a nonimmunogenic peptide comprise (a) a peptide-lipid complex optionally associated with a mixture of  $\geq 1$  phospholipids and  $\geq 1$  sterols, wherein the peptide-lipid complex comprises a nonimmunogenic amphipathic peptide covalently bound to a lipid; (b) the above mixture wherein the peptide in the complex is a hybrid peptide composed of a nonimmunogenic amphipathic peptide conjugated to  $\geq 1$  other peptides; and (c)  $> 1$  peptide-lipid complexes in the above described mixture. The nonimmunogenic human immunodeficiency virus peptide His-Arg-Pro-Gly-Gly-Gly-Asp-Met-Arg-Asp-Asn-Trp-Arg-Ser-Glu-Leu-Tyr-Lys-Cys-NH<sub>2</sub> (I) was made immunogenic by synthesizing it contiguous to an amphipathic peptide to form the peptide His-Arg-Pro-Gly-Gly-Gly-Asp-Met-Arg-Asp-Asn-Trp-Arg-Ser-Glu-Leu-Tyr-Lys-Tyr-Lys-Tyr-Val-Lys-Ile-Glu-Pro-Leu-Gly-Val-Ala-Pro-Thr-Lys-Ala-Lys-Arg-Arg-Val-Val-Gln-Arg-Glu-Lys-Arg-Cys-NH<sub>2</sub>, which was then reduced and conjugated with derivatized phosphatidylethanolamine (PE) contained in a mixture with sphingomyelin, **phosphatidylcholine**, **phosphatidylserine**, and **cholesterol**. I when conjugated to PE in the same mixture did not produce an immune response.

L13 ANSWER 9 OF 9 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 98:67476 CA

TITLE: Membrane-active properties of **glycoproteins** from liver tissue, liver plasma membranes, and kidney sodium-potassium ATPase

AUTHOR(S): Kremlev, I. N.; Potselueva, M. M.; Mirsalikhova, N. M.

CORPORATE SOURCE: Inst. Biol. Fiz., Pushchino, USSR

SOURCE: Deposited Doc. (1981), VINITI 5845-81, 27 pp. Avail.: VINITI

DOCUMENT TYPE: Report

LANGUAGE: Russian

AB The effects were studied of Ca<sup>2+</sup>, temperature, and lipid composition (total brain

lipids-cholesterol, oxidized cholesterol,  $\alpha$ -monoolein-cholesterol, total brain lipids-**phosphatidylserine-cholesterol**, or **phosphatidylcholine**) on lipid bilayer transmembrane elec. potential modification by liver plasma membrane, mitochondrial or microsomal **glycoproteins** with identical electrophoretic mobilities, and by kidney Na<sup>+</sup>,K<sup>+</sup>-ATPase (I). The modifying capacity of the **glycoproteins** was highly dependent on the lipid composition, surface charge, and phase state of the bilayer. In modified membranes, a transition was observed between cation (K<sup>+</sup>) and anion (Cl<sup>-</sup>) selective states. Apparently, transporting particles with a given selectivity undergo structural rearrangement leading not only to the formation of transporting particles with greater or less selectivity with respect to the given ions, but to transitions between states with different selectivities. Ion channels formed by the **glycoproteins** had a conductivity of 250 nS. From the biochem. and membrane characteristics of these **glycoproteins**, it is proposed that they are identical. **Glycoprotein** localization in I complexes and the function of I

ion-binding sites are discussed.